REMARKS

Reconsideration of this application is respectfully requested.

Status of the Claims

The dependency of claims 80 and 82 has been corrected. Claim 2-23, 36, 39-41, 43, 45-51, 53-57, 59, 66, 71,73, 75, 77, 80-82, 84 and 86-90 are pending and at issue.

Obviousness Rejection

Claims 2-23, 36, 39-41, 43, 45-51, 53-57, 59, 66, 71, 73, 75, 77, 80-82, 84 and 86-90 stand rejected under 35 U.S.C. 103(a) as obvious over International Publication No. WO 03/004001 ("WO '001") in view of US Patent No. 6,576,259 ("Yamashita") and the Merck Index entry for tacrolimus ("Merck"). The Examiner contends that it would have been obvious to use tacrolimus and hydroxypropyl methylcellulose (HPMC) in the process described in WO '001 in view of Yamashita. Applicants respectfully disagree.

The present claims call for (i) dispersing tacrolimus in a first composition comprising polyethylene glycol (PEG) and poloxamer, (ii) spraying the first composition onto a second composition (such as lactose), and then (iii) adding a release-rate modifier (such as hydroxypropyl methylcellulose) by dry mixing. *See* claim 59.

WO '001 is completely silent regarding tacrolimus. Further, WO '001 does not teach or suggest adding a release-rate modifier, such as hydroxypropyl methylcellulose, after the dispersion has been sprayed onto a second composition. Indeed, the Examiner acknowledges that "compositions of tacrolimus and HPMC with the PEG and poloxamer ingredients are not taught by [WO '001]." *See* Office Action at page 3.

Yamashita does not cure the deficiencies of WO '001. As noted above, the present claims require dry-mixing a release-rate modifier with a composition that has previously been formed by spraying a dispersion of tacrolimus, PEG and poloxamer onto a second composition. Yamashita

does not teach or suggest dry-mixing a release-rate modifier, such as hydroxypropyl methylcellulose, with a composition comprising tacrolimus, PEG and poloxamer. Furthermore, Yamashita does not teach or suggest adding a release-rate modifier, such as hydroxypropyl methylcellulose, to the tacrolimus containing composition after the composition has been sprayed onto lactose.

Rather, and in contrast to the present claims, Yamashita teaches that HPMC is directly added to and in intimate contact with the tacrolimus (i.e., before the tacrolimus has been sprayed onto lactose). *See*, e.g., Example 1 of Yamashita. For instance, in Example 1 of Yamashita, HPMC is added directly to an ethanolic solution of tacrolimus. The tacrolimus/HPMC mixture is then subsequently mixed with lactose. *See* Examples 2-5 of Yamashita.

Indeed, in the December 15, 2009 Office Action, the Examiner notes that Example 12 of Yamashita discloses directly mixing tacrolimus and HPMC 2910. The Examiner also states that in Example 16 of Yamashita "the solid material … **was then dry-mixed with lactose** and filled into a capsule." *See* December 15, 2009 Office Action at page 8 (emphasis added).

Therefore, Yamashita does not teach or suggest preparing a particulate composition by spraying a dispersion of tacrolimus, PEG and poloxamer onto a second composition (such as lactose), and subsequently dry-mixing the spray dried product with HMPC. One of ordinary skill in the art, upon reading Yamashita in combination with WO '001, would not have dry-mixed HPMC with a spray-formed mixture of tacrolimus, PEG, poloxamer and lactose, since the tacrolimus would not be in intimate contact with the HPMC, as taught by Yamashita.

The tacrolimus melting point disclosure in Merck does not cure any of the deficiencies in either WO '001 or Yamashita noted above.

Accordingly, WO '001, Yamashita and Merck, when taken alone or in any combination fail to disclose or suggest the presently claimed process in which a mixture of tacrolimus, PEG and poloxamer is sprayed onto lactose, and then subsequently dry-mixed with HPMC.

Furthermore, because the compositions taught by WO '001 and Yamashita are prepared by a different process from that presently claimed, the compositions of the cited references are,

necessarily, structurally different from the compositions presently claimed in product-by-process claims 64, 84 and 90. As stated above, there is no teaching or suggestion in the cited references that would lead one of ordinary skill in the art to the presently claimed methods. Therefore, product-by-process claims 64, 84 and 90 are also not obvious over a combination of WO '001, Yamashita and Merck.

For at least the foregoing reasons, the present claims are not obvious over the cited references. Applicants respectfully request, therefore, that the rejection be withdrawn.

CONCLUSION

Based on the above amendments and arguments, this application is believed to be in condition for allowance, which is earnestly solicited. If there are remaining issues that the Examiner believes could be addressed by conducting an interview or entering an Examiner's Amendment, the Examiner is cordially invited to contact the undersigned agent to discuss such issues.

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Respectfully submitted,

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